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Acetogenic Isoquinoline Alkaloids. XXIII.* Structure of the Naphthyl Isoquinoline Alkaloid Dioncophylline A

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Abstract. (1*R*,3*R*,7*S*)-7-[1-(4,5-Dimethoxy-2-methyl)naphthyl]-8-hydroxy-1,3-dimethyl-1,2,3,4-tetrahydroisoquinoline, $C_{24}H_{27}NO_3 \cdot CH_2Cl_2$, $M_r = 462.4$, orthorhombic, $P2_12_12_1$, $a = 11.032$ (2), $b = 12.420$ (3), $c = 17.080$ (8) Å, $V = 2340.3$ Å³, $Z = 4$, $D_x = 1.31$ Mg m⁻³, $\lambda(\text{Mo } K\alpha) = 0.71069$ Å, $\mu = 0.3$ mm⁻¹, $F(000) = 976$, $T = 290$ K, final $R = 0.063$, for 1617 observed reflections. The structure (constitution and relative configuration) is the same as established recently by spectroscopic, chiroptical, synthetic and degradative methods. A semi-empirical energy minimization calculation yields a structure very close to that of the X-ray analysis.

Introduction. Dioncophylline A (Bringmann, Rübenacker, Jansen, Scheutzw & Aké Assi, 1990), previously 'triphyophylline' (Bruneton, Bouquet, Fournet & Cavé, 1976), is one of the main alkaloids of the West African medicinal plant (Cooper & Record, 1931) *Triphyophyllum peltatum* (Dioncophyllaceae). Most recently, it was isolated for the first time from an Ancistrocladaceae species, *Ancistrocladus abbreviatus* Airy Shaw, along with the corresponding *N*-methyl derivative (Bringmann, Lisch, Reuscher, Aké Assi & Günther, 1991). Structurally, it belongs to the increasing novel group of naphthyl isoquinoline alkaloids (Bringmann, 1986), biosynthetically intriguing natural products of apparently acetogenic origin. We have recently been able to establish the complete stereostructure of dioncophylline A as shown in Fig. 1 (Bringmann, Rübenacker, Jansen, Scheutzw & Aké Assi, 1990; Bringmann, Jansen, Reuscher, Rübenacker, Peters & von Schnering, 1990), with (*R*) configurations at C(1) and C(3), and with (*S*) configuration at the stereogenic biaryl linkage, thus completing and revising the structure as published earlier (Bruneton, Bouquet, Fournet & Cavé, 1976). Unambiguous evidence for this structure was obtained from (1) extensive 1- and

2D NMR experiments (Bringmann, Rübenacker, Jansen, Scheutzw & Aké Assi, 1990) [constitution and relative configuration at C(1) versus C(3)], (2) CD spectroscopy (Bringmann, Rübenacker, Jansen, Scheutzw & Aké Assi, 1990) [absolute configuration at the axis], (3) total synthesis (Bringmann, Jansen, Reuscher, Rübenacker, Peters & von Schnering, 1990) [absolute configurations at C(1) and C(3)], (4) a novel atropisomer-differentiating cyclization reaction, which synthetically links the axis to the stereogenic centres (Bringmann, Jansen & Busse, 1991) [relative configuration at the axis], and (5) a degradation method recently described (Bringmann, Rübenacker, Jansen, Geuder & Aké Assi, 1991; Bringmann, Geuder, Rübenacker & Zagst, 1991) [absolute configurations at C(1) and C(3)].

As dioncophylline A is the first representative of the Dioncophyllaceae alkaloids to be fully structurally elucidated, an ultimate proof of this structure by an X-ray crystal analysis was desirable.

Many attempts to obtain appropriate crystals of dioncophylline A failed owing to insufficient quality. Although the crystal used showed a strong decrease in intensity with increasing diffraction angle and thus was not perfect, it was possible to measure enough reflections to get a reliable structure solution, which confirms the constitution and the relative configuration of dioncophylline A.

Experimental. Platy white crystals of dioncophylline A, crystallized from dichloromethane/ethanol, $0.5 \times 0.2 \times 0.1$ mm. Enraf-Nonius CAD-4 computer-controlled single-crystal diffractometer, graphite-

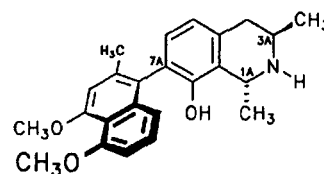


Fig. 1. Structural formula of dioncophylline A.

* Part XXII: Bringmann, Geuder, Rübenacker & Zagst (1991).

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monochromated Mo $K\alpha$ radiation, ω/θ scan, scan speed from $1-4^\circ \text{ min}^{-1}$, the ratio of peak to background counting time was 2:1. Cell parameters from setting angles of 23 reflections having $3 \leq 2\theta \leq 25^\circ$. Data collection at 290 K: index ranges $-14 \leq h \leq 0$, $-16 \leq k \leq 0$, $0 \leq l \leq 22$ with $3 \leq 2\theta \leq 58^\circ$, 2 standard reflections ($\bar{2}64$, $1\bar{3}\bar{3}$) measured every 60 min showed only random deviations from mean intensity, no absorption correction, 3197 reflections measured of which 1617 observed with $F_o^2 > 2.0\sigma(F_o^2)$.

Structure solved by *SHELXS86* (Sheldrick, 1986). Other programs used were from Nonius *SDP* package. In the final cycles of least-squares refinement all non-H atoms anisotropic. All H atoms calculated (0.95 \AA), 280 parameters refined, $\sum w(|F_o| - |F_c|)^2$ minimized with $w = 4[(F_o)^2/(\sigma I)^2 + P(F_o)^2]$, $P = 0.04$. $R = 0.063$, $wR = 0.061$, max. shift to e.s.d. in the final cycle = 0.03 , goodness of fit $S = 0.515$, $\Delta\rho_{\text{max}} = 0.33 (6)$, $\Delta\rho_{\text{min}} = -0.26 (6) \text{ e \AA}^{-3}$, scattering factors taken from *International Tables for X-ray Crystallography* (1974, Vol. IV). No abnormal displacement factors were found.

Furthermore, we have calculated the structure of dioncophylline A, using semi-empirical methods (Dewar's AM1 method; Dewar, Zoebisch, Healy & Stewart, 1985), to give the nearest energy minimized conformation of the molecule, starting from the X-ray data.

Discussion. The title compound crystallizes with one solvent molecule (dichloromethane) per dioncophylline A unit. Final atomic coordinates are reported in Table 1, interatomic distances and bond angles are presented in Table 2.* Bond lengths, bond angles

* Lists of structure factors, anisotropic thermal parameters, least-squares planes and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53871 (20 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

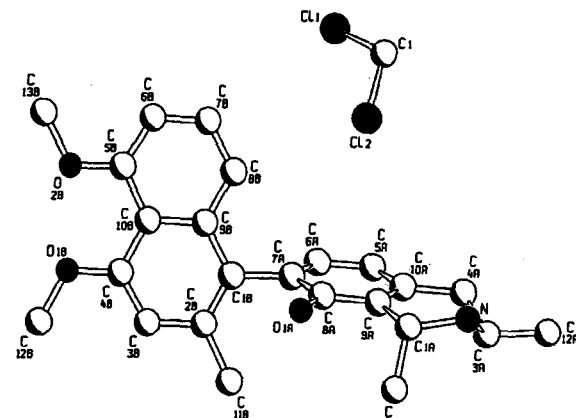


Fig. 2. *SCHAKAL86* (Keller, 1988) plot of dioncophylline A.

Table 1. *Positional parameters and isotropic thermal parameters with e.s.d.'s in parentheses*

	x	y	z	$B_{eq}(8\pi^2\text{\AA}^2)$
N	0.2931 (5)	0.3242 (5)	0.0971 (4)	3.1 (1)
C(3A)	0.2467 (7)	0.4359 (6)	0.0964 (5)	3.6 (2)
C(4A)	0.2464 (6)	0.4743 (6)	0.0128 (4)	3.3 (2)
C(5A)	0.4004 (6)	0.5190 (6)	-0.0918 (5)	3.1 (2)
C(6A)	0.5117 (7)	0.5051 (6)	-0.1278 (4)	3.2 (2)
C(7A)	0.5932 (7)	0.4297 (6)	-0.1013 (4)	3.1 (2)
C(8A)	0.5623 (7)	0.3665 (6)	-0.0366 (4)	3.1 (2)
C(9A)	0.4501 (6)	0.3835 (5)	0.0014 (4)	2.5 (1)
C(10A)	0.3690 (6)	0.4586 (6)	-0.0273 (4)	2.7 (1)
C(11A)	0.5062 (7)	0.3566 (7)	0.1421 (5)	4.0 (2)
C(12A)	0.1194 (7)	0.4354 (8)	0.1315 (5)	4.9 (2)
O(1A)	0.6359 (4)	0.2889 (4)	-0.0059 (3)	3.7 (1)
C(1B)	0.7192 (6)	0.4227 (6)	-0.1370 (4)	2.8 (1)
C(2B)	0.8171 (7)	0.4587 (6)	-0.0972 (4)	3.2 (2)
C(3B)	0.9329 (6)	0.4576 (6)	-0.1336 (5)	3.4 (2)
C(4B)	0.9484 (7)	0.4198 (6)	-0.2078 (4)	3.1 (1)
C(5B)	0.8564 (7)	0.3347 (6)	-0.3285 (5)	3.6 (2)
C(6B)	0.7550 (7)	0.2961 (7)	-0.3662 (5)	4.2 (2)
C(7B)	0.6429 (8)	0.3011 (7)	-0.3296 (5)	4.4 (2)
C(8B)	0.6292 (7)	0.3424 (6)	-0.2561 (4)	3.3 (2)
C(9B)	0.7317 (7)	0.3827 (6)	-0.2144 (4)	3.1 (1)
C(10B)	0.8481 (6)	0.3796 (6)	-0.2519 (4)	2.9 (1)
C(11B)	0.8110 (7)	0.5005 (7)	-0.0136 (4)	4.5 (2)
C(12B)	1.1588 (7)	0.4591 (8)	-0.2017 (5)	5.5 (2)
C(13B)	0.9798 (9)	0.2934 (9)	-0.4397 (5)	6.4 (3)
O(1B)	1.0592 (5)	0.4166 (5)	-0.2429 (3)	4.0 (1)
O(2B)	0.9686 (5)	0.3301 (5)	-0.3609 (3)	4.9 (1)
Cl(1)	0.7003 (3)	0.7583 (3)	0.8678 (2)	7.98 (8)
Cl(2)	0.6683 (3)	0.6984 (3)	0.7065 (2)	9.4 (1)
Cl(1)	0.7665 (7)	0.7004 (8)	0.7861 (6)	6.2 (3)
C(1A)	0.4252 (6)	0.3177 (6)	0.0744 (4)	3.0 (1)

Anisotropically refined atoms are given in form of the isotropic equivalent displacement parameter defined as:

$$B_{eq} = (4/3) [a^2\beta(1,1) + b^2\beta(2,2) + c^2\beta(3,3) + ab(\cos\gamma)\beta(1,2) + ac(\cos\beta)\beta(1,3) + bc(\cos\alpha)\beta(2,3)].$$

Table 2. *Bond distances (Å) and bond angles (°) with e.s.d.'s in parentheses*

N—C(3A)	1.48 (1)	C(2B)—C(3B)	1.42 (2)
N—C(1A)	1.51 (1)	C(2B)—C(11B)	1.52 (2)
C(3A)—C(4A)	1.51 (2)	C(3B)—C(4B)	1.36 (2)
C(3A)—C(12A)	1.53 (2)	C(4B)—C(10B)	1.43 (2)
C(4A)—C(10A)	1.53 (1)	C(4B)—O(1B)	1.36 (1)
C(5A)—C(6A)	1.38 (1)	C(5B)—C(6B)	1.38 (2)
C(5A)—C(10A)	1.38 (1)	C(5B)—C(10B)	1.42 (2)
C(6A)—C(7A)	1.37 (2)	C(5B)—O(2B)	1.36 (1)
C(7A)—C(8A)	1.40 (1)	C(6B)—C(7B)	1.39 (2)
C(7A)—C(1B)	1.52 (1)	C(7B)—C(8B)	1.37 (2)
C(8A)—C(9A)	1.41 (1)	C(8B)—C(9B)	1.43 (2)
C(8A)—O(1A)	1.37 (1)	C(9B)—C(10B)	1.44 (2)
C(9A)—C(10A)	1.38 (1)	C(12B)—O(1B)	1.41 (1)
C(9A)—C(11A)	1.52 (1)	C(13B)—O(2B)	1.43 (1)
C(11A)—C(1A)	1.54 (1)	Cl(1)—C(1)	1.73 (1)
C(1B)—C(2B)	1.35 (2)	Cl(2)—C(1)	1.74 (2)
C(1B)—C(9B)	1.42 (2)		
C(3A)—N—C(1A)	112.4 (9)	C(3B)—C(2B)—C(11B)	117. (1)
N—C(3A)—C(4A)	108 (1)	C(2B)—C(3B)—C(4B)	121. (1)
N—C(3A)—C(12A)	108.1 (1)	C(3B)—C(4B)—C(10B)	121. (1)
C(4A)—C(3A)—C(12A)	112. (1)	C(3B)—C(4B)—O(1B)	122. (1)
C(3A)—C(4A)—C(10A)	112 (1)	C(10B)—C(4B)—O(1B)	117. (1)
C(6A)—C(5A)—C(10A)	121. (1)	C(6B)—C(5B)—C(10B)	121. (1)
C(5A)—C(6A)—C(7A)	121. (1)	C(6B)—C(5B)—O(2B)	122. (1)
C(6A)—C(7A)—C(8A)	119. (1)	C(10B)—C(5B)—O(2B)	117. (1)
C(6A)—C(7A)—C(1B)	120.4 (9)	C(5B)—C(6B)—C(7B)	120. (1)
C(8A)—C(7A)—C(1B)	120.5 (9)	C(6B)—C(7B)—C(8B)	122. (1)
C(7A)—C(8A)—C(9A)	120. (1)	C(7B)—C(8B)—C(9B)	120. (1)
C(7A)—C(8A)—O(1A)	123.7 (9)	C(1B)—C(9B)—C(8B)	121. (1)
C(9A)—C(8A)—O(1A)	117 (1)	C(1B)—C(9B)—C(10B)	121. (1)
C(8A)—C(9A)—C(10A)	120 (1)	C(8B)—C(9B)—C(10B)	118. (1)
C(8A)—C(9A)—C(1A)	117.1 (9)	C(4B)—C(10B)—C(5B)	125. (1)
C(10A)—C(9A)—C(1A)	122.5 (9)	C(4B)—C(10B)—C(9B)	117 (1)
C(4A)—C(10A)—C(5A)	121. (1)	C(5B)—C(10B)—C(9B)	119. (1)
C(4A)—C(10A)—C(9A)	120.0 (9)	C(4B)—O(1B)—C(12B)	118.0 (9)
C(5A)—C(10A)—C(9A)	119 (1)	C(5B)—O(2B)—C(13B)	119. (1)
C(7A)—C(1B)—C(2B)	121 (1)	Cl(1)—C(1)—Cl(2)	119. (7)
C(7A)—C(1B)—C(9B)	119 (1)	N—C(1A)—C(9A)	110.9 (8)
C(2B)—C(1B)—C(9B)	120. (1)	N—C(1A)—C(11A)	110.6 (9)
C(1B)—C(2B)—C(3B)	120. (1)	C(9A)—C(1A)—C(11A)	110.1 (9)
C(1B)—C(2B)—C(11B)	123. (1)		

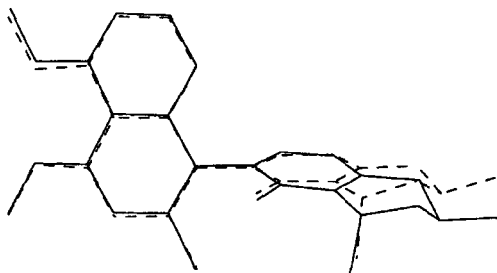


Fig. 3. Superimposed view of dioncophylline A molecules as determined by X-ray diffraction (full lines) and by energy minimization (dashed lines).

and torsion angles of dioncophylline A show no unusual features. The relative configuration at the three stereo-elements (two centres and the axis) is in full agreement with the stereostructure as established earlier (Bringmann, Jansen, Reuscher, Rübenacker, Peters & von Schnering, 1990). The absolute configuration, as shown in Fig. 2 was not determined here, but was adopted from our work mentioned above. The dihedral angle between the two aromatic parts of the biaryl system is 110.2° .

As the AM1 energy minimization calculation (Dewar, Zoebisch, Healy & Stewart, 1985) shows, the molecule in the crystal is close to one of the local energy minima, and hence there are no greater distortions in the molecule that might arise from intermolecular interactions (Fig. 3).

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References

- BRINGMANN, G. (1986). *The Naphthyl Isoquinoline Alkaloids In The Alkaloids*, Vol. 29, edited by A. BROSSI, pp. 141–184. New York: Academic Press.
- BRINGMANN, G., GEUDER, T., RÜBENACKER, M. & ZAGST, R. (1991). *Phytochemistry*, **30**, 2067–2070.
- BRINGMANN, G., JANSEN, J. R. & BUSSE, H. (1991). *Justus Liebigs Ann. Chem.* In the press.
- BRINGMANN, G., JANSEN, J. R., REUSCHER, H., RÜBENACKER, M., PETERS, K. & VON SCHNERING, H. G. (1990). *Tetrahedron Lett.* **31**, 643–646.
- BRINGMANN, G., LISCH, D., REUSCHER, H., AKÉ ASSI, L. & GÜNTHER, K. (1991). *Phytochemistry*, **30**, 1307–1310.
- BRINGMANN, G., RÜBENACKER, M., JANSEN, J. R., GEUDER, T. & AKÉ ASSI, L. (1991). *Planta Med.* **56**, 495–496.
- BRINGMANN, G., RÜBENACKER, M., JANSEN, J. R., SCHEUTZOW, D. & AKÉ ASSI, L. (1990). *Tetrahedron Lett.* **31**, 639–642.
- BRUNETON, J., BOUQUET, A., FOURNET, A. & CAVÉ, A. (1976). *Phytochemistry*, **15**, 817–818.
- COOPER, G. P. & RECORD, S. J. (1931). *Bull. Yale Univ. Sch. For.* **31**, 1–153.
- DEWAR, M. J. S., ZOEBSCH, E. G., HEALY, E. & STEWART, J. J. P. (1985). *J. Am. Chem. Soc.* **107**, 3902–3909.
- KELLER, E. (1988). *SCHAKAL88. A FORTRAN Program for the Graphic Representation of Molecular and Crystallographic Models*. Kristallographisches Institut der Universität, D-7800 Freiburg, Germany.
- SHELDRICK, G. M. (1986). *SHELXS86*. Program for the automatic solution of crystal structures. Univ. of Göttingen, Germany.

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Structure of L-Lysinamide Dihydrochloride. A New Conformation of the Lysine Side Chain

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Abstract. L-Lysinamide dihydrochloride, $C_6H_{17}N_3O^{2+} \cdot 2Cl^-$, $M_r = 218.14$, monoclinic, $C2$, $a = 19.998$ (52), $b = 4.942$ (26), $c = 15.997$ (32) Å, $\beta = 138.04$ (29)°, $V = 1057.1$ Å³, $Z = 4$, $D_x = 1.371$ g cm⁻³, $\lambda(Mo K\alpha) = 0.71069$ Å, $\mu = 5.9$ cm⁻¹, $F(000) = 464$, room temperature, $R = 0.067$ for 599 observed reflections. No head-to-tail hydrogen bonds between terminal N and C groups are observed in the structure. All suitable H atoms are involved in at

least one hydrogen bond. The lysine side chain conformation (g^-tg^-t) has not been previously observed.

Introduction. Amino acid derivatives and small peptide structures contain detailed information which is useful in protein conformation studies. The structure determination of L-lysine dihydrochloride is part of a project that involves the struc-

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